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Exhibit A

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants: AOKI et al) Examiner: Anish Gupta
Serial Number: 09/490,756) Art Unit: 1653
Filed: January 24, 2000)
For: METHOD FOR TREATING DYSTONIA)
WITH BOTULINUM TOXIN TYPE B) Irvine, California

DECLARATION UNDER 37 C.F.R. SECTION 1.132

I, MITCHELL F. BRIN, declare as follows:

1. I am over the age of twenty one, competent to testify in a court of law, and could and would testify to the matters set forth below before the United States Patent and Trademark Office, if required to do so.

2. I understand that this declaration will be used to assist prosecution of United States patent application serial number 09/490,756, including to assist to overcome a rejection in the November 8, 2000 office action in serial number 09/490,756 based upon a mode or capability of operation attributed to a reference.

3. I graduated from the University of Pennsylvania in 1975 with a bachelor of arts in biology (Magna Cum Laude and Phi Beta Kappa) and I received an M.D. degree from the Columbia College of Physicians and Surgeons. I completed neurology and fellowship training at the Columbia University Neurological Institute. In 1994, I joined the Mount Sinai Medical Center as an Associate Professor and Director of the Movement Disorders Program.

I was most recently, attending Physician and Associate Professor of Neurology at the Mount Sinai School of Medicine in New York where I also served as Director of Movement Disorders and held the Bachmann-Strauss Endowed Chair in Neurology. I have directed numerous neurological research programs relating to use of a botulinum toxin in the treatment of movement disorders, such as dystonia.

I was one of the first investigators to examine the use of botulinum toxin for the treatment of medical disorders and I pioneered the use of botulinum toxin for the

treatment of dystonias, including blepharospasm and other debilitating neurological disorders. I have designed and conducted double blind studies examining the use of botulinum toxin for numerous conditions, and have conducted a number of multicenter studies for uses of botulinum toxin.

I founded the American Academy of Neurology course on botulinum toxin, and I have organized numerous courses and symposia on botulinum toxin, and has published extensively on this subject.

I hold many appointments and affiliations, including President and Founder of WE MOVE, an international professional and patient educational not-for-profit organization that focuses on movement disorders. I also serve on the board of directors of the Bachmann-Strauss Dystonia and Parkinson Foundations and the Exceptional Parent Foundation. I serve on the review board of the United States Pharmacopeial Convention and the Steering Committee of the World Congress on Disabilities. I am a member of the American Academy of Neurology Section on Movement Disorders and Co-Founder of the Dystonia Study Group.

I also serve on the editorial and peer-review boards of numerous scientific journals and on the steering committee of the World Congress on Disabilities. I am the recipient of many awards including being elected a Fellow to the American Academy of Neurology; recipient of the FDA's Commissioner's Special Citation for my work with neurological movement disorders; and a Distinguished Service and Honor Award from the American Otolaryngology Society.

A partial list of my publications is attached to this declaration as Appendix A.

By training and experience I am an expert in the therapeutic use of the botulinum toxins, including use of botulinum toxin type B to treat dystonia.

4. I am currently employed by Allergan, Inc, the assignee of the above-identified patent application, as Vice President, *Botox*[®]/Neurology. In this capacity, I oversee the *Botox*[®] (botulinum toxin type A purified neurotoxin complex) development portfolio, and direct clinical programs for uses of the botulinum toxins.

5. I am the co-author of Jankovic J, and Brin M., *Therapeutic Uses of Botulinum Toxin*, New Eng J. Med, 1186-1194;1991 (the "Jankovic reference").

6. The Jankovic reference discusses therapeutic uses of *only* type A botulinum toxin. As of the April 25, 1991 date of the Jankovic reference it was completely unknown as to whether or not botulinum toxin type B would have any therapeutic efficacy in human. Indeed, as far as I am aware, the first reported use of type B botulinum toxin in humans did not occur until 1995.

7. Additionally, the Jankovic reference does not state that botulinum type B can be used as an alternative or in place of botulinum type A, although it does speculate on page 1189, that other botulinum toxins, immunologically distinct from the type A toxin, may have some utility to treat patients who have become non-responsive to type A toxin due to a development of antibodies to the type A toxin.

8. In my opinion, prior to December 28, 1993, it would have been foolhardy and dangerous to use botulinum toxin type B to treat patients with dystonia, such as cervical dystonia, in light of the complete lack of clinical experience with the type B toxin as of that date. Certainly, the 1991 Jankovic reference does not teach, suggest, motivate or recommend use of botulinum toxin type B by physicians to treat any dystonic patients.

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that any such willful false statements may jeopardize the validity of the above-identified application or any patent issuing therefrom.

Executed this 8 day of February 2001, at Irvine, California.



Mitchell F. Brin

ATTACHMENT A**PUBLICATIONS OF MITCHELL F BRIN****A. Original, Peer Reviewed Publications**

1. Wormser GP, Donath J, Kennish A, Brin MF, Sanders M. Fatal pneumonia. *NYS J Med* 1981;1088-1089.
2. †Brin MF, Fetell MR, Green PHA, Kayden HJ, Hays AP, Behrens MM, Baker H. Blind loop syndrome, vitamin E malabsorption, and spinocerebellar degeneration. *Neurology* 1985;35:338-342.
3. Bressman S, Fahn S, Eisenberg M, Brin M, Maltese W. Biotin-responsive encephalopathy with myoclonus, ataxia, and seizures. *Adv Neurology* 1985;43:119-125
4. Lange DJ, Warner C, Brin M, List T, Fahn S, Lovelace RE. Botulinum toxin therapy: distant effects on neuromuscular transmission. *Muscle Nerve* 1985;8:624-625.
5. Blitzer A, Lovelace RE, Brin MF, Fahn S, Fink ME. Electromyographic findings in focal laryngeal dystonia (spastic dysphonia). *Ann Oto, Rhino, and Laryngoscope* 1985; 94:591-594.
6. † Brin MF, Pedley TA, Lovelace RE, Emerson RG, Gouras P, MacKay C, Kayden HJ, Levy J, Baker H. Electrophysiological features of abetalipoproteinemia: functional consequences of vitamin E deficiency. *Neurology* 1986; 36:669-673.
7. Breakefield XO, Bressman SB, Kramer PL, Ozelius LO, Moskowitz C, Tanzi R, Brin MF, Hobbs W, Kaufman D, Kidd KK, Fahn S, Gusella J. Linkage analysis in a family with dominantly inherited torsion dystonia: Exclusion of the pro-opiomelanocortin and glutamic acid decarboxylase genes, and other chromosomal regions using DNA polymorphisms. *J Neurogenetics* 1986;3:159-175.
8. Burke RE, Brin MF, Fahn S, Bressman SB, Moskowitz C. An analysis of the clinical course of non-Jewish autosomal dominant torsion dystonia. *Movement Disorders* 1986;1:163-178.
9. Blitzer A, Brin MF, Fahn S, Lange D, Lovelace RE. Botulinum toxin for the treatment of spastic dysphonia. *Laryngoscope* 1986;96:1300-1301.
10. Lange DJ, Brin M, Warner C, Fahn S, Lovelace RE. Distant effects of local

injections of botulinum toxin. *Muscle Nerve* 1987;10:552-555.

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13. Blitzler AB, Brin MF, Fahn S, Lovelace RE. Localized injections of botulinum toxin for the treatment of focal laryngeal dystonia (spastic dysphonia). *Laryngoscope* 1988;98:193-197.
14. Blitzler AB, Brin MF, Fahn S, Lovelace RE. Clinical and laboratory characteristics of laryngeal dystonia: A study of 110 cases. *Laryngoscope* 1988;98:636-640.
15. Vatassery GT, Brin MF, Fahn S, Kayden HJ, Traber MG. Effect of high doses of dietary vitamin E on concentrations of vitamin E in several brain regions, plasma, liver and adipose tissue. *J Neurochem* 1988;51:621-623.
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17. Younger DS, Chou S, Hays AP, Lange DJ, Emerson R, Brin MF, Thompson H, Rowland, LP. Primary lateral sclerosis: A clinical diagnosis re-emerges. *Arch Neurol* 1988;45:1304-7.
18. Blitzler A, Brin MF, Fahn S. Botulinum toxin injection for the treatment of oromandibular dystonia. *Ann Oto Rhino Laryngol* 1989;98:93-97.
19. † Brin MF, Blitzler A, Fahn S, Gould W, Lovelace RE. Adductor laryngeal dystonia (spastic dysphonia): Treatment with local injections of botulinum toxin (BOTOX). *Movement Disorders* 1989;4:287-296.
20. Ozelius L, Kramer PL, Moskowitz CB, Kwaitkowski J, Brin MF, Bressman SB, Schuback DE, Falk CT, Risch N, de Leon D, Burke RE, Haines J, Gusella JF, Fahn S, Breakefield XO. Human gene for torsion dystonia located on chromosome 9q32-q34. *Neuron* 1989;2:1427-1434.
21. Bressman SB, de Leon D, Brin MF, Risch N, Burke RE, Greene PE, Shale H, Fahn S. Idiopathic dystonia among Ashkenazi Jews: Evidence for autosomal dominant inheritance. *Ann Neurol* 1989;26:612-620.
22. † Brin MF, Fahn S, Loftus S, McMahon D, Flaster E. Relationship between dose of vitamin E administered and blood level. *Ann NY Acad Sci* 1989;570:421-424.

23. Parkinson Study Group. DATATOP: A multi-center controlled clinical trial in early Parkinson's disease, *Archives of Neurology* 1989; 46:1052-1060.
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31. Saint-Hilaire MH, Burke RE, Bressman SB, Brin MF, Fahn S. Delayed onset dystonia due to perinatal or early childhood asphyxia. *Neurology*, 1991;41:216-222.
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33. Lange DJ, Rubin M, Greene PE, Kang UJ, Moskowitz CB, Brin MF, Lovelace RE, Fahn S. Distant effects of locally injected botulinum toxin: A double-blind study of single fiber EMG changes. *Muscle Nerve* 1991;14:672-675.

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45. † Borg-Stein J, Pine ZM, Miller JR, Brin MF. Botulinum toxin for the treatment of spasticity in multiple sclerosis. *Am J Phys Med Rehabil* 1993;72:364-368.
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 68. *,† Blitzer A, Binder WJ, Aviv JE, Keen MS, Brin MF. The management of hyperfunctional lines with botulinum toxin: A collaborative study of 210 injection sites in 162 patients. *Arch Otolaryngol* 1997;123:389-392.
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